PROCESS FOR TEH PREPARATION OF MODIFICATION I OF N-(1-METHYLETHYLAMINOCARBONYL) -4-(3-METHYLPHENYLAMINO)-3-PYRIDINESULFONAMIDE

znd This application is a 371 application to PCT/HR03/00036 filed July 7,2003.

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nvention relates to the preparation of modification I of *N*-(1-methylethyl
l)-4-(3-methylphenylamino)-3-pyridinesulfonamide (in the further text
tion designated by its generic name "torasemide").

Torasemide is a new potent diuretic in the class of so-called "loop" diuretics and is described in DE patent 25 16 025 (Example 71) as 3-isopropylcarbamylsulfonamide-4-(3'-methyl)-phenylamino pyridine. Structurally, it is completely different from diuretics of the same class such as e.g. furosemide, bumetanide and azosemide. Besides diuretic properties it also possesses antihypertensive ones.

As a diuretic of Henle's loop it is interesting as an agent for preventing heart or heart tissue damages caused by metabolic or ionic abnormalities associated with ischemia, in the treatment of thrombosis, angina pectoris, asthma, hypertension, nephroedema, pulmonary edema, primary and secondary aldosteronism, Bartter's syndrome, tumours, glaucoma, decrease of intraocular pressure, acute or chronic bronchitis, in the treatment of cerebral edema caused by trauma, ischemia, concussion of the brain, metastases or epileptic attacks and in the treatment of nasal infections caused by allergens.

Hitherto, some crystal modifications of torasemide have been known: modification I [*Acta Cryst.* B34 (1978), 1304-1310], modification II [*Acta Cryst.* B34 (1978), 2659-2662], modification III (US patent 6,166,045), modification N (US patent 6,399,637), modification V (PLIVA; PCT/WO 01/87841), modification V (TEVA; PCT/WO 01/10441), as well as an amorphous modification of PLIVA (PCT/WO 01/70694), an amorphous modification of TEVA (PCT/WO 01/10441) and Dupont 2 solvate adducts (PCT/WO 01/10441). Crystal modifications I, II and N differ in single cell